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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/096,589	06/12/1998	ROBERT J. SCHNEIDER	5914-65	1985

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/096,589	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-55 have been canceled. Claims 56-68 are at issue and are present for examination. Applicants amendment of 4/1/05 canceling all previous claims and adding new claims 56-68 canceled all subject matter to the elected and previously examined invention and thus could be held non-responsive. However as all new claims recite subject matter as examined in the parent applicant, the examiner has decided to allow the shift and has examined the instant claims. Applicants are cautioned however that similar shifts in the claimed subject (including returning to the previously examined subject matter) matter will not necessarily be allowed by the examiner and any attempt to introduce claims to both groups will result in all claims to subject matter patentably distinct to that currently examined being withdrawn from consideration.

Claims 56-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "small organic molecule" in claims 56-58 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and

one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 68 is indefinite in the recitation "a homolog or analog of c-Src" as the specification does not define what characteristics define either a "homolog" or and "analog".

Claims 56-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating HBV or inhibiting HBV replication by administering a compound which decreases the activity of Src kinase or Fyn kinase, does not reasonably provide enablement for methods of treating HBV or inhibiting HBV replication by administering a compound which decreases the activity of any Src kinase family member. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification establishes that upon HBV infection that the cellular levels of Src and Fyn kinase activity are increased (see Example 6) and that these kinases are necessary for *in vitro* viral replication (see Example 9). As such a skilled artisan would reasonably expect that inhibitors of these kinase would be useful for the treatment of HBV. However, the specification provides no basis for a skilled artisan to

reasonably believe that other Src family kinase members are involved in HBV infection and replication and therefore, a skilled artisan would not reasonably expect inhibitors of other Src kinase family members to be useful as claimed. The Src kinase family is a very large family of kinases which share a common structural organization. However, Src family kinases are expressed in a highly diverse spectrum of cell types and are involved in a diverse spectrum of biological processes many of which involve only one or a few individual family members. (See for example Thomas et al. for a general review of Src family kinases and Eliceiri et al. and Qian et al. for specific examples of distinct activities among Src kinase family members) It is well known in the art that there are only three Src kinase family members which are expressed in most tissues i.e., Src, Yes, and Fyn (see page 515 of Thomas et al.) while all other Src kinase family members are expressed almost exclusively in hematopoeitic tissues. As HBV is a disease which is not associated with hematopoeitic tissues, these Src family members are highly unlikely to be involved in HBV infection and/or replication. Furthermore, while redundancy in function is often found among Src kinase family members, many functions are found in only one or a few family members such that a showing that Src kinase and Fyn kinase appear to be involved in HBV replication

would not lead a skilled artisan to conclude that all Src kinase family members are similarly involved absent a showing that this is in fact the case.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 57 and 65-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Levitzki et al. (WO 91/16892).

Levitzki et al. teach a method of inhibiting cell proliferation in a patient comprising administering a benzylidenemalononitrile derivative. While Levitzki et al. do not teach that the disclosed method would inhibit HBV infection or replication, this result is an inherent effect of the method disclosed by Levitzki et al.

Claims 57 and 65-68 are rejected under 35 U.S.C. 102(e) as being anticipated by Dow et al. (US Patent 5,593,997).

Dow et al. teach a method of treating tyrosine kinase dependent diseases in a patient comprising administering a pyralozopyrimidine derivative. While Dow et al. do not teach that the disclosed method would inhibit HBV infection or replication, this result is an inherent effect of the method disclosed by Dow et al.

Claims 57 and 65-68 are rejected under 35 U.S.C. 102(a) as being anticipated by Tang et al. (WO 96/40629).

Tang et al. teach a method of treating tyrosine kinase dependent diseases in a patient comprising administering a tryphostin derivative. While Tang et al. do not teach that the disclosed method would inhibit HBV infection or replication, this result is an inherent effect of the method disclosed by Tang et al.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a),

the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 57 and 65-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yokoyama et al.

Yokoyama et al. teach that angelmicin B inhibits differentiation of human myeloid leukemia cells and suggest that it would be useful in the treatment of acute promyelocytic leukemia. Therefore, it would have been obvious to one of ordinary skill in the art to administer angelmicin B to a patient with acute promyelocytic leukemia. While Yokoyama et al. do not teach that the suggested method would inhibit HBV infection or replication, this result is an inherent effect of the method suggested by Yokoyama et al.

Claims 59-61 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al (US Patent 5,593,997) in view of Hunter et al. (US Patent 5,994,341).

Dow et al. teach a method of inhibiting angiogenesis in a patient comprising administering a pyralozopyrimidine derivative. While Dow et al. do not teach that the disclosed method would inhibit HBV infection or replication, this result

is an inherent effect of the method disclosed by Dow et al. Dow et al. do not teach the further inclusion of additional antiviral agents in the composition.

Hunter et al. teach compositions of an anti-angiogenic agent and a polymeric carrier. Hunter et al. further teach that such compositions may additionally comprise antiviral agents, interferons, interleukins, or corticosteroids such as prednisone (see column 15-16).

Therefore, it would have been obvious to one of ordinary skill in the art to use the pyralozopyrimidine derivatives of Dow et al. as the anti-angiogenic factor in the compositions of Hunter et al. Furthermore, it would have been obvious to one of ordinary skill in the art to include additional compounds such as antiviral agents, interferons, interleukins, or corticosteroids such as prednisone as taught by Hunter et al.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 56-68 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,420,338. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 56-68 herein and claims 1-6 of U.S. Patent No. 6,420,338 are both directed to methods of treating HBV comprising administering a compound which inhibits a Src kinase family member. The claims differ in that claims 56-58 and 65-68 herein recites that the compound used is a small organic compound which inhibits any Src kinase family member whereas claims 1-6 of U.S. Patent No. 6,420,338

recites that the compound used is any compound which inhibits Src kinase specifically. Claims 59-64 herein further recite the use of additional antiviral compounds in combination with the Src kinase family member inhibitor. Claims 3-6 of U.S. Patent No. 6,420,338 and 65-66 herein specify the use of specifically one or more of a tryphostin, a pyrazolopyrimidine, a benylidenemalononitrile, or an angelmicin or salts thereof as the Src kinase family member inhibitor. As such these claims will anticipate claims 56-58 and 65-68 herein. Furthermore, it would have been obvious to one of skill in the art given the methods of Claims 1-6 of U.S. Patent No. 6,420,338 to use the Src kinase inhibitors as recited in these claims in combination with one or more compounds which were previously known in the art for the treatment of HBV, as the use of the combination would likely enhance the therapeutic effect of either alone. As each of the compounds recited in claims 59-64 herein were known in the art at the time of the instant invention for the treatment of HBV, it would have been obvious to use them in combination with the Src kinase inhibitors as taught by Claims 1-6 of U.S. Patent No. 6,420,338.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is

reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on

access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rebecca Prouty
Primary Examiner
Art Unit 1652